



**Automated therapy production using
3D printing of isoleucine for treatment
of MSUD:
World first single-centre prospective study**

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[@FabRx_3DP](#)



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- Maple Syrup Urine Disease (MSUD) is a rare, severe metabolic disorder (1 in 185,000 births)
- Deficiency in branched chain alpha-keto acid dehydrogenase (BCKD) complex

Symptoms:

- Sweet-smelling urine
- Vomiting
- Lethargy
- Developmental delay
- If poorly managed= seizures, coma, death



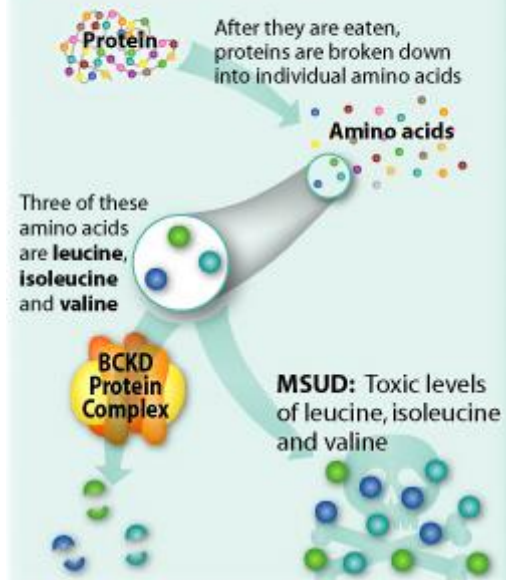
Healthy urine

MSUD urine

Treatments =

Dietary restriction of BCAAs
 Strict diet of isoleucine (and other BCAAs)
 BCAA blood level monitoring
 Patients required to weigh out powders

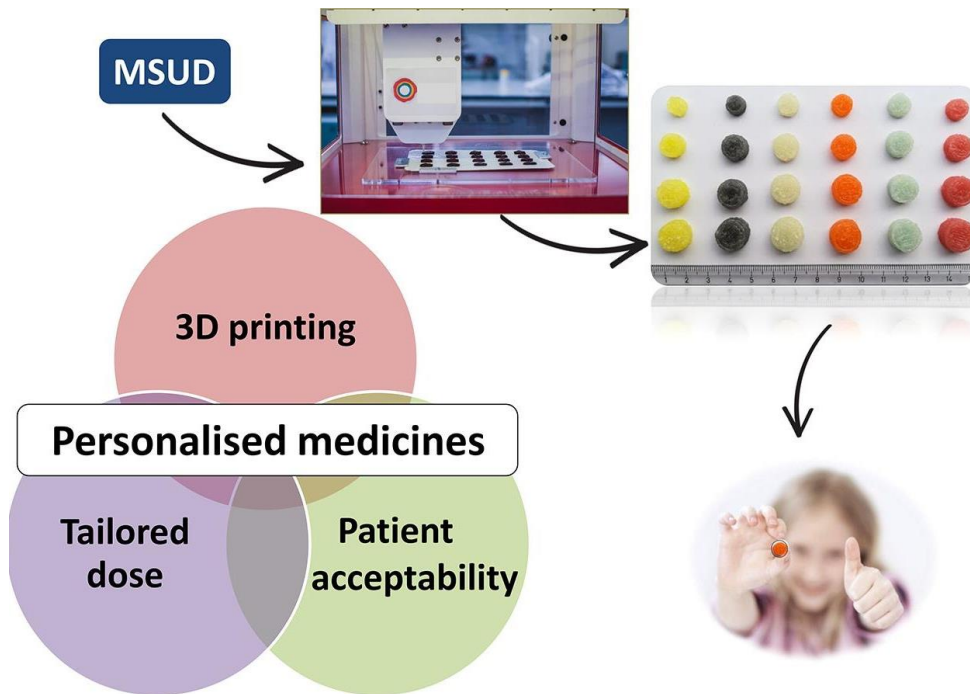
People with MSUD Have a Defective BCKD Protein Complex



Normally, the BCKD protein complex breaks down leucine, isoleucine and valine.

People with MSUD have a defective BCKD protein complex, so toxic levels of leucine, isoleucine and valine build up in their bodies.

- Integrate FabRx 3D Printer into a hospital pharmacy setting (Clinic University Hospital, Spain)
- Treat four paediatric patients with personalised isoleucine dosages for MSUD
 - Conventional capsules vs. printlets
- Evaluate therapy control and medicine acceptability across 6 months of treatment



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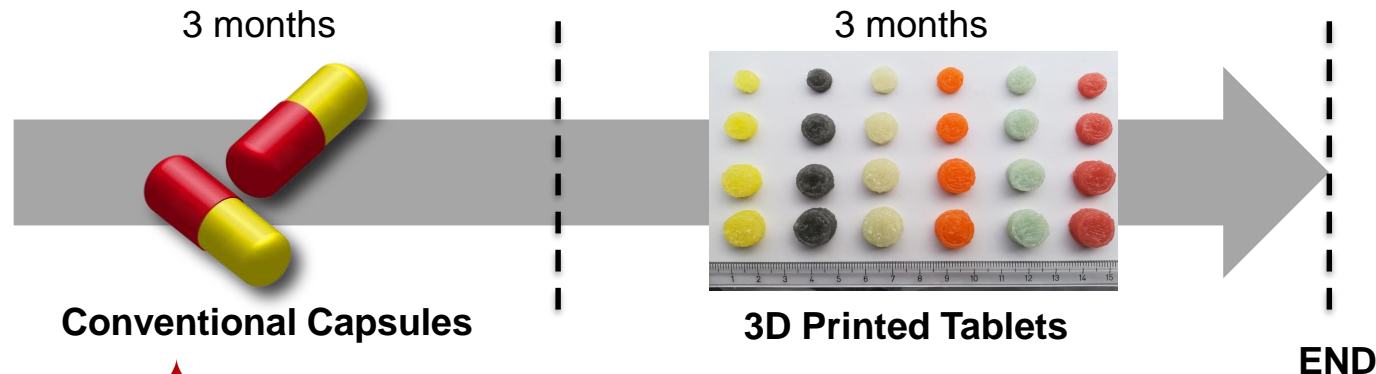
Patient Recruitment:

4 patients with MSUD
(2M, 2F; 3-16 yrs)

Patient	Gender	Age (Y-M)	Isoleucine dosage (mg)	Rx Instructions
1	M	5y 0m	50	M, W, F
2	F	3y 8m	100	Daily
3	M	16y 1m	200	Daily
4	F	10y 1m	100-150	Daily

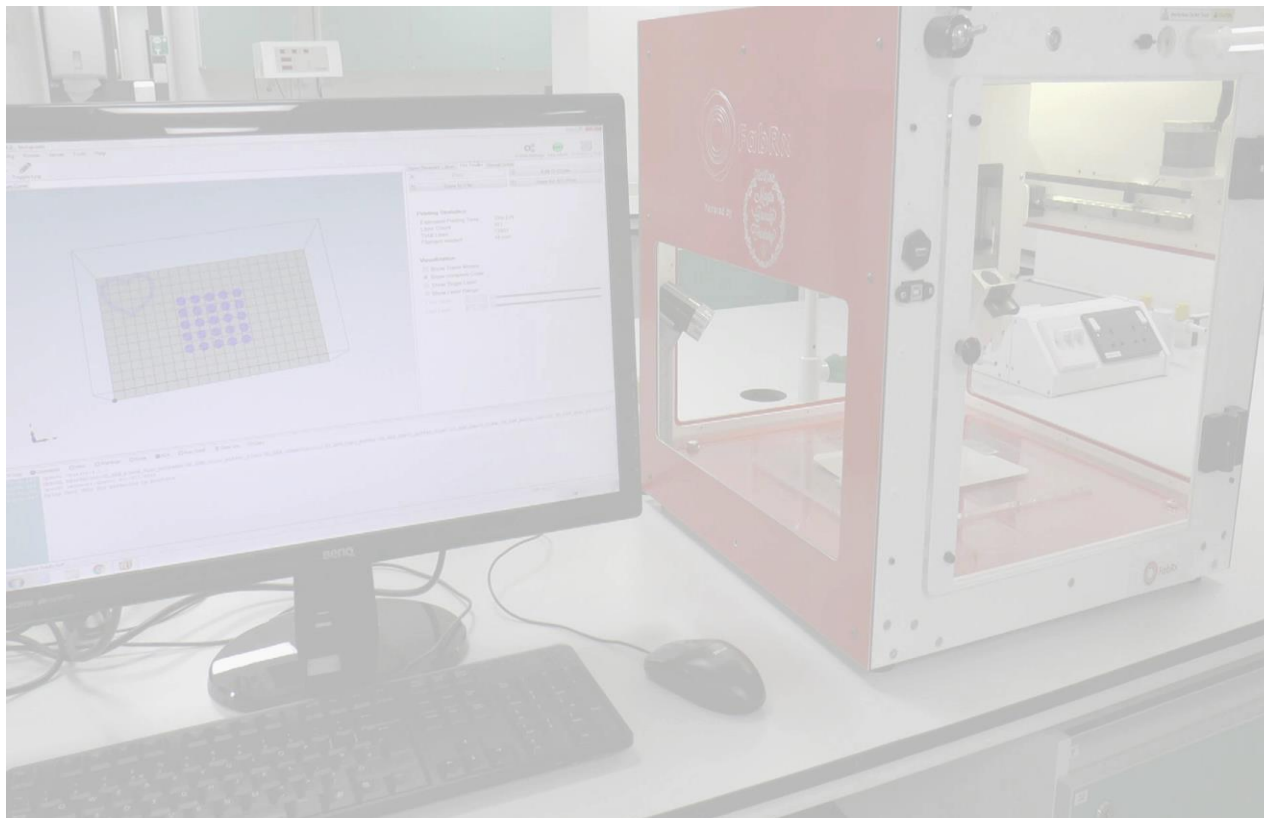
Study Design:

Single centre,
prospective design



Evaluated for:

- Isoleucine levels (regularly)
- Medicine acceptability (2 weeks)





6 x flavours
4 x doses

Evaluated for:

Drug levels

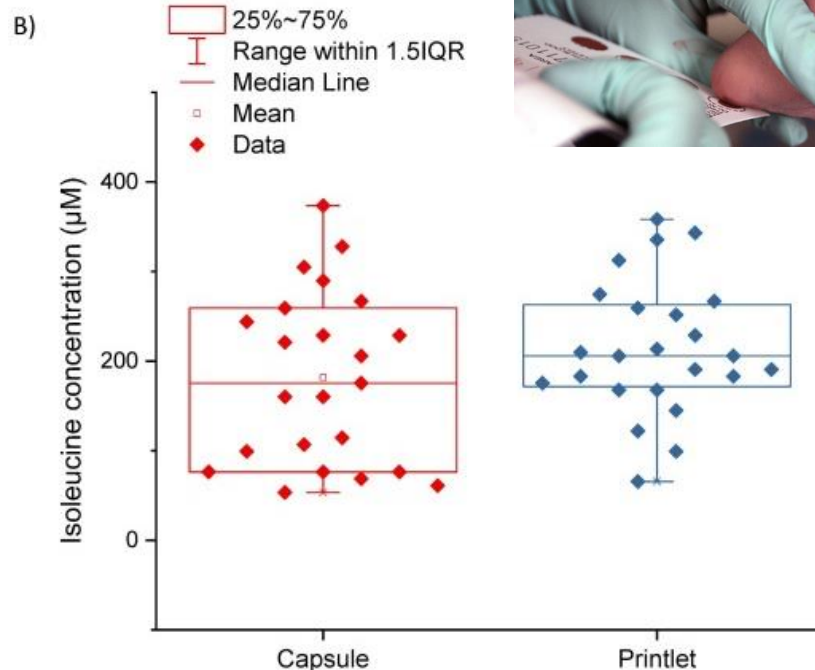
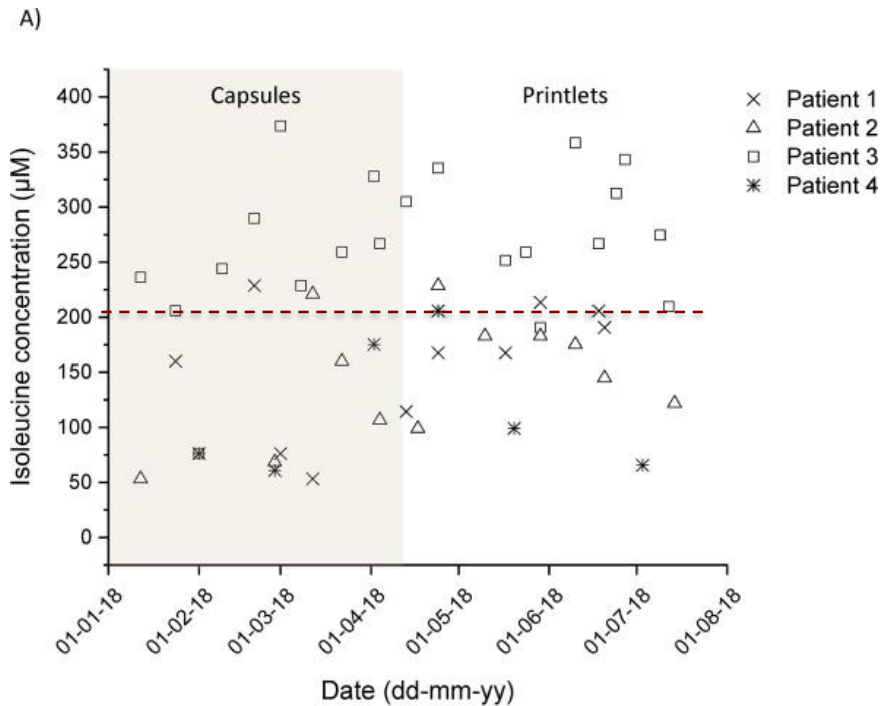
Acceptability



Heel dried blood spot (DBS)

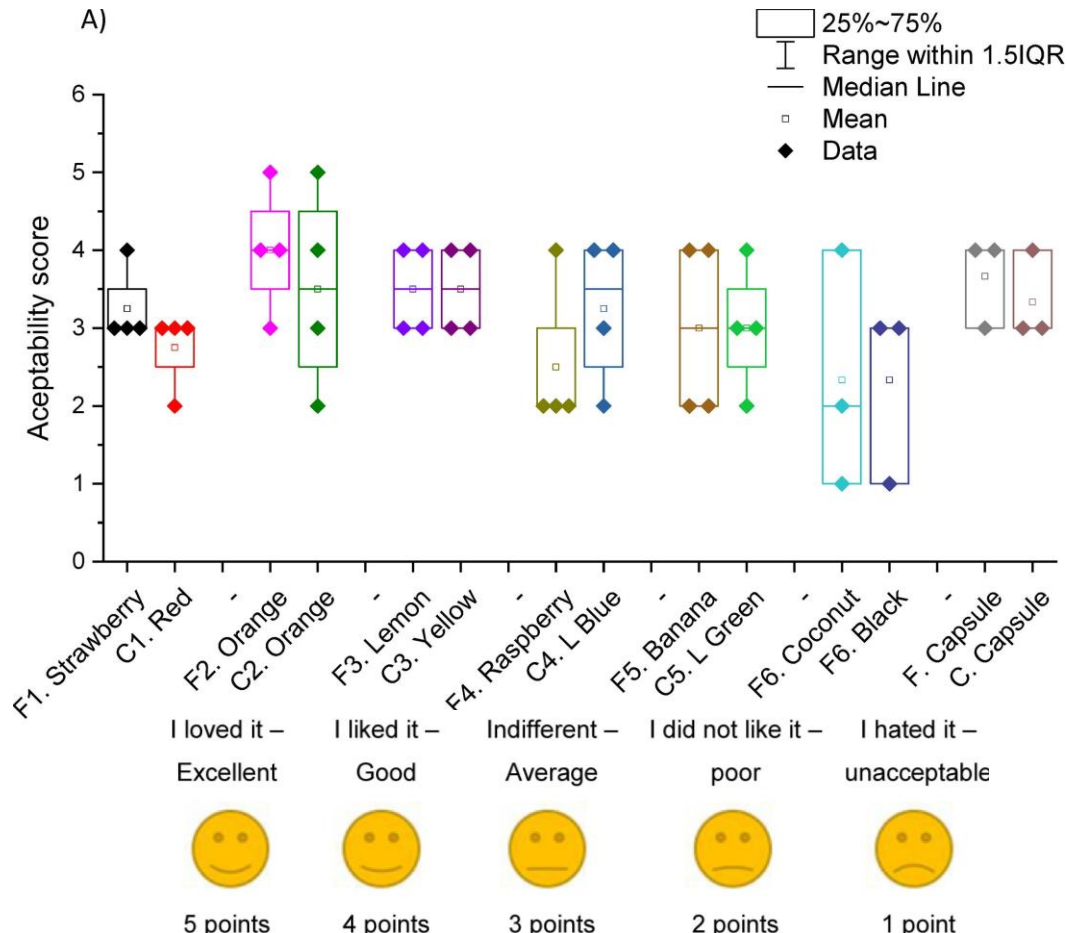
PRO

Parent observations



Target = $200\mu\text{M} - 400\mu\text{M}$

Conclusions = 3D printed formulations enabled a tighter control in target range

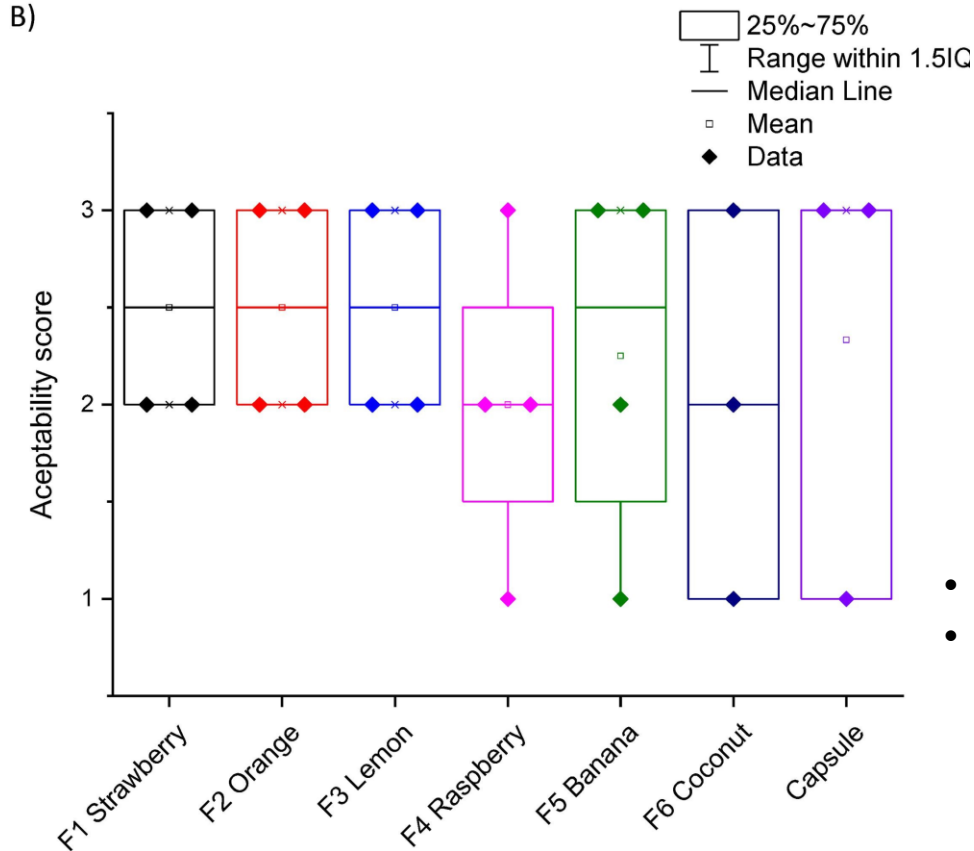


- Majority were well accepted
- Most accepted were:
 - Lemon-yellow, orange



- Least accepted were:
 - Coconut & raspberry





Please rate the participants facial expression:

Positive face or offers signs of approval	3 points
No facial expression	2 points
Signs of distress (grimacing, “scrunching up” face, squinting, signs of disapproval)	1 point

- All formulations well accepted
- Capsules, coconut & raspberry least



- Conducted a world first clinical study in comparing FabRx printlets vs. conventional dosage forms
- Printlets enabled a tighter control over isoleucine blood levels
- Majority of flavours / colours well accepted
- Provides further evidence base for use of printed personalised medicines

FabRx GMP Printer



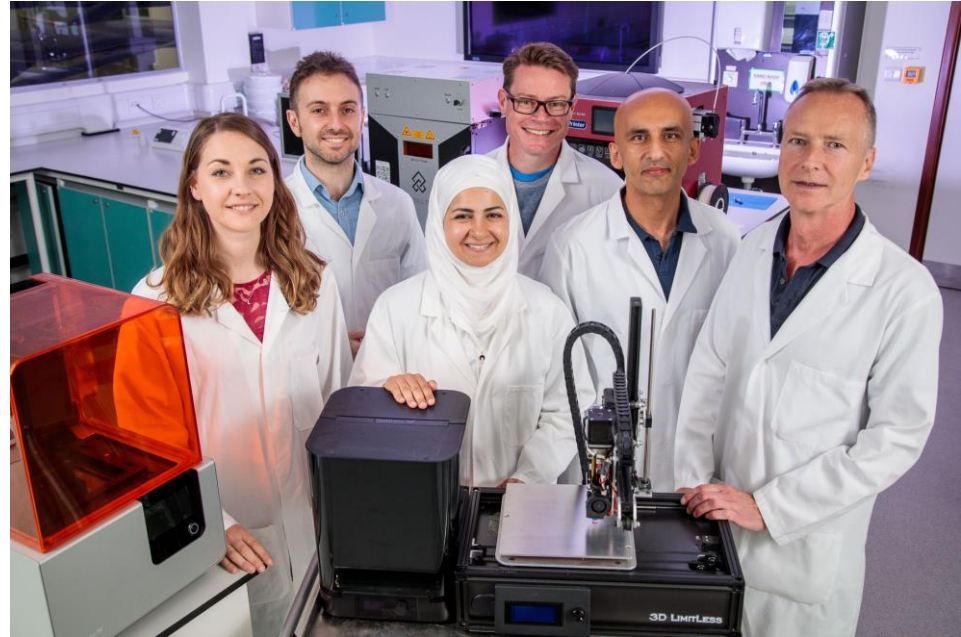
Characteristics:

- User-friendly software
- Portable and versatile printing platform
- Affordable cost
- Ensure drug product quality
- Real-time-release



We work with
Innovate UK

- Alvaro Goyanes (study)
- FabRx team
- Farhan Taherali (UCL)
- Christine Madla (UCL)
- Clinical staff at Clinic University Hospital
 - Dr. Couce
 - Dr. Lamas



Thank you!

